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An exploratory survey of professionals on the use of stored tissue samples from minors for genetic research

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ABSTRACT. The ethical aspects of the use of stored tissue samples collected from minors are of topical interest. However, the views of professionals working in the field of genetics have not been investigated in depth anywhere. We conducted a survey among 194 such professionals in Belgium. This list was composed of the members of the High Council for Anthropogenetics, supplemented with all professionals working in the field of genetics that we found on the websites of the eight Belgian centers of human genetics and of the associated university registries. We achieved a response rate of 35.5%. The vast majority (92%) think that research on stored tissue samples is useful. Most respondents stated that parental consent is valid (82.5%), and 76.5% thought that children should also be given the right to assent when they are able to comprehend the implications of the storage of biological samples and of genetic research. Slightly more than half put the age at which young people can understand storage or

research rather high: 16-18 years (51 and 53.1%, respectively). Although there is some consensus in the literature that donors should be allowed to give broad consent for future research on their biological samples, only 47.6% in our survey thought that parents should be allowed to consent to any future research on their children's samples. The aim of our study was to give some basis for future ethical reflections and policies on the subject of stored tissue samples from minors for genetic research. We concluded that a large majority of Belgian researchers and clinicians in the field of genetic research think research on stored tissue samples from minors is useful. They also think that parental consent for such research is valid, but that children should be allowed to assent as they grow older.

Key words: Survey; Ethics; Biobank; Genetic research; Consent

INTRODUCTION

The use of stored tissue samples from minors has gained some attention lately after the publication of a policy forum in Science (Gurwitz et al., 2009). In this policy forum, it is stated that population biobanks involving children and their tissue raise specific ethical issues that are not covered by the general discussion, which assumes that participants are adults that can autonomously decide on participation. A recently published literature review has confirmed this (Hens et al., 2009a). The main theme in the existing literature is consent: is parental consent sufficient or valid for storing biological samples from children in biobanks? Should children be allowed to give assent ('permission') when they have reached an age at which they can understand the implications of storage and research? What is this age? Are parents allowed to give broad consent for research on the stored tissue samples of their children?

There is already a substantial body of empirical literature on stored tissue samples in general. This literature is based on surveys querying the general population (Hoeyer et al., 2004; Kettis-Lindblad et al., 2006), patients (Pentz et al., 2006; Hull et al., 2008; Pulley et al., 2008; Goldenberg et al., 2009) or biobank participants (Hoeyer, 2003). The views of professionals on the ethical questions regarding stored tissue samples are far less investigated. Ruiz-Canela et al. (2009) did a survey of researchers in the USA and Spain on the issue of informed consent and the subjects' right to know the results of a study. With regard to stored tissue samples from minors, we found three surveys (Joseph et al., 2008; Goldenberg et al., 2009; Jackson et al., 2009), two qualitative studies investigating children's views (Williamson et al., 2004; Goodenough et al., 2004) and a focus group study (Kaufman et al., 2008). Only one study queried the viewpoints of professionals on the issue of tumor banking: Jackson et al. (2009) did a survey among pediatric oncology health professionals on the usefulness of tissue banking and the issue of consent in pediatric research on tumors.

Given the lack of publications in this specific area, we found it necessary to query the opinions of Belgian professionals who work with DNA samples, with regard to this subject. We asked about their opinion on the usefulness of research on stored tissue samples of children, the validity and scope of parental consent, the need for a child's assent and the age at which they thought children could understand storage of biological samples and research on these samples. This paper is a report of our findings.

METHODS

To compile the list of addressees of our survey, we took the names of the members of the High Council for Anthropogenetics, an official Belgian body composed of geneticists from all different centers in Belgium with the task of coordinating the activities of the eight Belgian centers for human genetics. We supplemented this list with professionals whom we found on the websites of all the eight Belgian centers of human genetics and of the associated university registries. We took a broad approach to the selection of participants: if the website did not specify otherwise, we assumed the people enlisted were involved in or had a professional opinion on stored tissue samples for genetic research.

We created a structured questionnaire based on a review of the ethics literature on stored tissue samples (Hens et al., 2009b). The survey was reviewed by one medical doctor, one researcher in genetics and one researcher in biochemistry. These reviewers did not participate in the final survey.

A total of 194 questionnaires were sent out via e-mail starting on September 11, 2008. We sent out 8 reminders during the period of September 2008 to September 2009, including one postal questionnaire. No monetary or other incentive was offered. We received six notifications that the person had left the institution. We received eight notifications of people stating they did not work in the field of genetic research and that they thought the questionnaire was not applicable to them. A total of 64 surveys were returned completed (response rate = 35.5%). We believe the rather low return rate can be attributed to different reasons. First, as we sent out the questionnaire to a rather broad audience, several recipients must have thought this was not applicable to them. Second, the questionnaire took 20 to 30 min to complete. We talked to some of the recipients, and they told us that their busy schedule did not allow them to complete questionnaires. Third, the low return rate for questionnaires among professionals in general is well known (Ruiz-Canela et al., 2009). As 95.3% of our respondents claimed that their institute stores biological samples for genetic research, and as 46.9% stated that their educational background was in science and 48.4% medicine, we still think that the data we gathered is representative of the viewpoints of professionals in the field of genetic research in Belgium.

Response implied informed consent. The questionnaires were coded upon receipt and processed using SPSS 16.0. We generated frequency tables and used the Fisher exact chi-square test to calculate significant relationships between the findings. When we found significance in findings, we indicated this below.

RESULTS

We collected the following biographical data of respondents: gender, year of birth, whether they have children, in which province (including Brussels) do they live, educational background, number of years involved in genetic research and whether the institute in which they work stores human biological samples for non-therapeutic research. We had a fairly even distribution of males and females (42.9 *vs* 57.1%), most of our respondents had children (80.6%) and the majority had been involved in genetic research for over 4 years (70.2% in all cases). The mean age of our respondents was 44 years (SD = 11; range = 24-69). An overview of these demographics can be found in Table 1.

Table 1. Biographical data.

Gender*	
Female	57.1%
Male	42.9%
Age (years)*	
21-30	11.3%
31-40	32.3%
41-50	35.5%
51-60	9.7%
61-70	11.3%
Have children*	
Yes	80.6%
No	19.4%
Province*, **	
Antwerpen	12.7%
Brabant Wallon	4.8%
Brussels	14.3%
Hainaut	4.8%
Liège	12.7%
Limburg	3.2%
Luxemburg	1.6%
Namur	0%
Oost-Vlaanderen	14.3%
Vlaams-Brabant	30.2%
West-Vlaanderen	1.6%
Educational background	
Science (biology, (bio)chemistry, (bio)engineering)	46.9%
Medicine	48.4%
Humanities	1.6%
Pharmacy	3.1%
Years involved in genetic research	
<1	3.1%
1-3	6.2%
4-6	39.1%
11-20	31.2%
Longer than 20	20.3%
Does the institute you work store human biological samples for further non-therapeutic research?*	
Yes	95.1%
No	4.9%

*As some respondents (maximum 3) skipped certain boxes, the valid percentages are given. **Including Brussels.

Our first set of questions was related to the usefulness of stored tissue samples from minors for research and to the need for parental consent and the assent of the child. The vast majority of respondents thought that genetic data from minors is useful for research (92%). They also thought that parental consent is valid (82.5%). However, the majority also believed that children should be given the opportunity to assent once they could understand the implications of storage and genetic research (76.5%). An overwhelming majority thought that young people should be given the right to withdraw their data from a collection when they reach the age of 18 (95.2%). Table 2 gives an overview of the findings for the first set of questions.

We also investigated the scope of parental consent. We asked for which types of research could parents give consent. The majority of respondents agreed that parents should be allowed to consent to either well-specified research (79.4%) or research for a specific condition (77.8%). A little less than half of them thought parents could consent to any possible research (47.6%). The results are in Table 3.

Table 2. Likert-scale questions about usefulness, consent and assent.

Genetic data from minors is useful for research*	Strongly agree	45.2%
	Agree	46.8%
	Neither agree nor disagree	6.5%
	Disagree	1.6%
	Strongly disagree	0%
Parental consent is sufficient for storage of biological samples for genetic research of any child who cannot assent ('give permission') because he or she cannot understand the nature of the research*	Strongly agree	20.6%
	Agree	61.9%
	Neither agree nor disagree	7.9%
	Disagree	3.2%
	Strongly disagree	6.3%
Once a child can understand the implications of biological sample storage and genetic research, he or she should be allowed to assent ('give permission')	Strongly agree	20.3%
	Agree	56.2%
	Neither agree nor disagree	6.2%
	Disagree	14.1%
	Strongly disagree	3.1%
A child should have the right to withdraw their data from a biological sample collection when he or she is 18 years old*	Strongly agree	33.3%
	Agree	61.9%
	Neither agree nor disagree	0%
	Disagree	3.2%
	Strongly disagree	1.6%

*As some respondents (maximum 3) skipped certain boxes, the valid percentages are given.

Table 3. To which type of research should parents be allowed to consent for their children?

Research that is well specified at the time of consent*	79.4%
Genetic research related to a specific gene*	58.7%
Genetic research related to a specific condition*	77.8%
Any possible future genetic research*	47.6%

*As one respondent skipped this question, the valid percentages are given.

We also investigated at which age respondents thought children were able to understand the implications of storage of biological samples and of genetic research. A small majority thought this age was 16-18 years for both the storage of samples (51.5%) as for the genetic research (53.1%). We found a correlation between the age of the respondents and the answers to the question about which age people can understand the implications of storage (Fisher exact test, P = 0.039). The results are in Table 4.

Table 4. Age of understanding.

From which age do you think children can understand the implications of storage of biological samples for future genetic research?	
0-3 years	0%
4-6 years	0%
7-9 years	1.6%
10-12 years	17.2%
13-15 years	29.7%
16-18 years	51.6%
From which age do you think children can understand the implications of genetic research?	
0-3 years	0%
4-6 years	0%
7-9 years	0%
10-12 years	14.1%
13-15 years	32.8%
16-18 years	53.1%

DISCUSSION

This study demonstrates that a large majority of researchers and clinicians in the field of genetic research think that research on stored tissue samples from minors is useful. They also thought parental consent is valid, but that minors should be given the opportunity to assent once they are able to understand the implications of the storage of biological samples and of genetic research. The age when minors would be able to do so was set quite high by a small majority: around 16-18 years. Respondents also thought people should be able to withdraw their data from a biological sample collection when they turn 18.

The need for assent from minors is consistent with the ethics literature (Holm, 2005; Helgesson, 2005; Hens et al., 2009a). It is seen as a general duty to include children in the decision making, at the moment that they can understand what is at stake. This is a right that is laid down in the United Nations Convention on the Rights of the Child (UN (United Nations), 1998) and can also be linked to the fact that in order to develop autonomy, a child should be able to exercise it (Helgesson, 2005). A small majority of our respondents suggested a fairly high age at which children can understand the implications of genetic research and the storage of their samples (16-18 years old). In a survey of clinical geneticists to decide at which age a minor can decide on having a carrier test, also this age (around 16) is given (Borry et al., 2008). There is, however, much discussion about the age at which a minor can understand genetic research. General literature regarding the capability of children to make decisions suggests that even at a very young age children can be involved in decision making (Alderson et al., 2006). However, with regard to genetic testing, others have found that even teenagers have difficulties grasping the full scope and impact of genetic information (Boddington and Gregory, 2008). Also, the legal situation in Europe on the position of minors in a health care setting is not straightforward. An overview of legal regulations shows that this position varies: the age and circumstances under which minors are allowed to make health care decisions vary in different countries, and is sometimes set as low as 14 (Portugal) (Stultiens et al., 2007). One could even question whether it is possible to establish a fixed threshold for assent or whether this is dependent on maturity and social context, and must be decided on a case-by-case basis (Wendler and Shah, 2003; Ashcroft et al., 2003). And, even if children have no thorough understanding of the implications at the moment that they are enrolled in research, do they not have the right to be informed in terminology that they can understand, even when they are below the official threshold for assent?

Our respondents almost unanimously agreed that donors should be given the opportunity to withdraw their data from a biological sample collection when they are 18 years old. This is in accordance to the ethics literature on the subject (Hens et al., 2009b). Holm (2005), for example, argues that as children have not been able to autonomously consent and give up the right to withdraw at the moment of donation, the right to withdraw for children is more important than for adults. It is less clear whether this entails a positive duty on the side of the researchers to recontact donors when they are 18 to inform them about their samples, or whether it can be left to the parents to inform their children of their participation.

A topic much discussed in the general ethics literature on stored tissue samples is the scope of consent. Should donors of biological samples be allowed to consent to any future research or should they be recontacted to give consent for each specific research? The study

by Ruiz-Canela et al. (2009) shows that professionals prefer a less restrictive consent. Also, a systematic review by Wendler (2006) has indicated that most donors would not mind giving one-time general consent. However, our respondents were somewhat more restrictive, as they in general preferred consent for well-specified research or research on specific diseases. The difference is the fact that we asked about the right of parents to consent for their children.

Whether they have this right is not often questioned in ethics literature (Hens et al., 2009a), but the fact that this is a proxy consent possibly limits the actual scope of the consent. How to best balance on the one hand feasibility and on the other hand respect for the rights of children to make their own decisions should be determined by policy makers of pediatric biobanks before enrolling donors.

Our study has several limitations. First, there is the fairly low response rate (35.5%), which may make our study not entirely representative of the Belgian professionals working with biological samples. Second, the section on biological samples from minors was only a part of the survey; this may or may not have influenced some of the answers; however, as we still obtained a fairly large sample of Belgian professionals in the field of genetics, and as this is a largely untrodden area, we think that our study can be the onset of a more thorough discussion.

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